

On page 9, at line 20, please replace the paragraph beginning, "Figures 6A-D" with the following paragraph:

--Figures 6A-D. Targeting of the *lats* locus by homologous recombination. (A) Sequence alignment of human *lats* (h-*lats*) (SEQ ID NO: 2) and mouse *lats* (m-*lats*, partial sequence) (SEQ ID NO: 9). Arrow indicates the point at which the mouse *lats* gene was disrupted. (B) Targeting vector for positive-negative selection of homologous recombinants at the *lats* locus, with restriction map and the structure of the targeted *lats* locus. The vector is represented by the second line from the top, while the wild-type and mutant (i.e., disrupted) *lats* alleles are indicated by the top and bottom lines, respectively. The BamHI sites are indicated by "B", the EcoRI sites are indicated by "R", and the EcoRV sites are indicated by "RV". Exons are represented by filled rectangles. A BamHI/EcoRV double digest generates a 3.5 kb fragment from the wild-type allele and a 5.8 kb fragment from the disrupted allele, both of which are recognized by the probe shown, which is not contained in the targeting vector. In the vector and the mutant allele, the PGK-TK gene cassette and the PGK-neo fragment are denoted by open boxes labeled accordingly. (C) Southern blot of genomic DNA isolated from individual embryonic stem cell clones. The genotypes of the clones are indicated above the lanes with the "+/" indicating wild-type clones, "+/-" indicating clones heterozygous for the mutant allele, and "-/-" indicating clones homozygous for the mutant allele. (D) Western blot using anti-h-*lats* polyclonal antibody on lysates from 13.5 dpc (days post coitus) mouse embryonic fibroblasts indicating the absence of *lats* protein in the knock-out mice. The genotype of the clones is indicated above the lanes as in panel C.

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REMARKS

Applicants have amended the Specification to include reference to International Application PCT/US99/19068, of which the present application is a national stage application. Also, pursuant to 37 C.F.R. § 1.78(a)(2), the first sentence of the specification indicates that International Application PCT/US99/19068 was published under PCT Article 21(2) in English.

Applicants have also amended the Specification to identify the sequences disclosed therein by their respective SEQ ID NOs as found in the Substitute Sequence Listing being submitted concurrently herewith. No new matter is introduced by virtue of these